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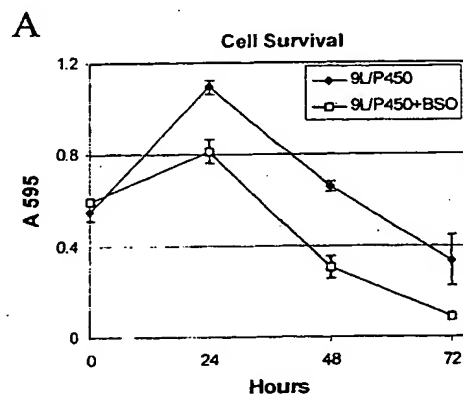
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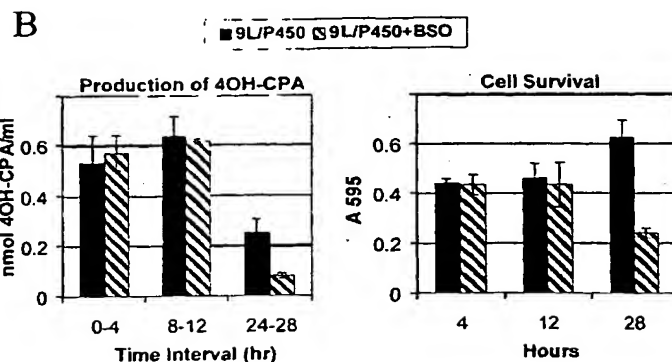
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[Continued on next page]

(54) Title: METHOD OF USING ANTI-APOPTOTIC FACTORS IN GENE EXPRESSION



(57) Abstract: The present invention is directed to methods of prolonging the expression of a heterologous gene (transgene) in a cell, preferably a malignant cell. This method can be used to increase the concentration of a chemotherapeutic agent in a target cellular environment. Preferably, the present invention relates to methods of inhibiting apoptotic cell death to enhance transgene expression, such as gene-directed enzyme/prodrug therapy.



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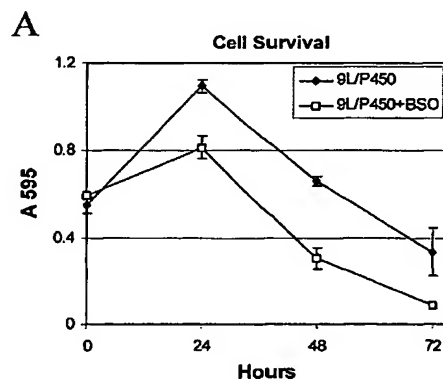
(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,

(72) Inventors; and

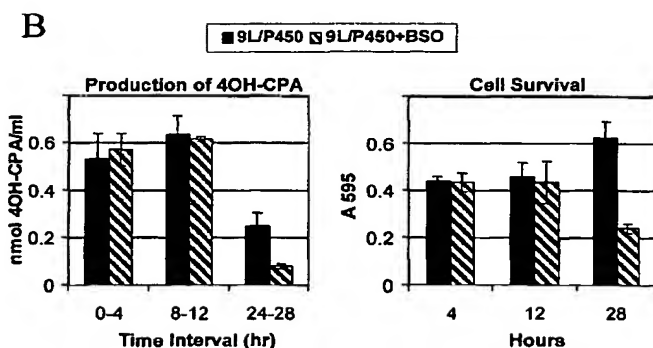
(75) Inventors/Applicants (for US only): **WAXMAN, David**,

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INTERNATIONAL SEARCH REPORT

International application No.

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A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61K 31/70; C12N 15/63; C07H 21/04 US CL : 514/44; 435/320.1, 455; 536/23.2, 23.4, 23.7 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 514/44; 435/320.1, 455; 536/23.2, 23.4, 23.7 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/46637 A2 (ARCH DEVELOPMENT CORPORATION) 22 October 1998, see pages 34-38 under the section Methods for the inhibition of apoptosis.	1
Y		2
Y	US 6,207,648 B1 (WAXMAN et al) 27 March 2001, see abstract and claims.	2
Y	US 5,688,773 A (CHIOCCA et al) 18 November 1997, see abstract and claims.	2
X,P	SCHWARTZ et al. Enhanced bystander cytotoxicity of P450 gene-directed enzyme prodrug therapy by expression of the antiapoptotic factor p35. Cancer Research. 01 December 2002, Vol. 62, pages 6928-6937, see the entire document, especially the abstract.	1-35
A	US 6,156,535 A (KORNELUK et al) 05 December 2000, see cols. 17-19.	1-35
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
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"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	
"P" document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search	Date of mailing of the international search report	
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Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer Quang Nguyen, Ph.D. Telephone No. (703) 308-0196	

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Continuation of B. FIELDS SEARCHED Item 3:

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Search terms: antiapoptotic, apoptosis inhibiting, inhibitor of apoptosis, prodrug therapy, GDEPT, enhanced, increased therapeutic, bystander.